SUPPORT FOR AMENDMENT

Claims 1 and 34 have been amended. No new matter has been added.

REQUEST FOR RECONSIDERATION

Drug release from polymeric implants is typically provided by a solution of a biodegradable polymer and a bioactive agent in a biocompatible solvent. The solution solidifies upon injection into the body to form a polymeric implant from which the agent is released. In some instances, this method yields zero-order release kinetics. However, zero-order release kinetics are not ideal for all therapies, and there is a need for biodegradable implants that can have a variety of drug release characteristics.

The present invention includes a composition for controlled release of a bioactive agent, comprising a biodegradable crystallizable polymer, a biodegradable amorphous polymer, a biocompatible solvent, and a bioactive agent. Crystallizable polymers, when crystallized, are semi-crystalline; and all semi-crystalline polymers are crystallizable.

In Table 1 in the Examples, a comparison is shown between a composition containing only a biodegradable amorphous polymer (PDLA, Example 5) and compositions which contain a biodegradable crystallizable polymer (PCL, Examples 1-4) alone or as a part of a combination with a biodegradable amorphous polymer. Figures 5 and 10, reproduced on the next page for convenience, illustrate the variation in release characteristics that can be provided by the presence of crystallizable polymer in the formulation.

Figure 5

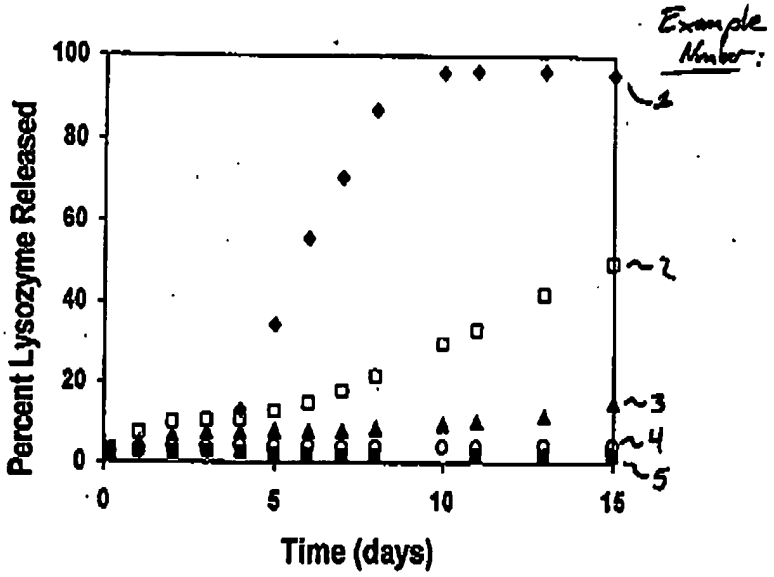

Figure 10

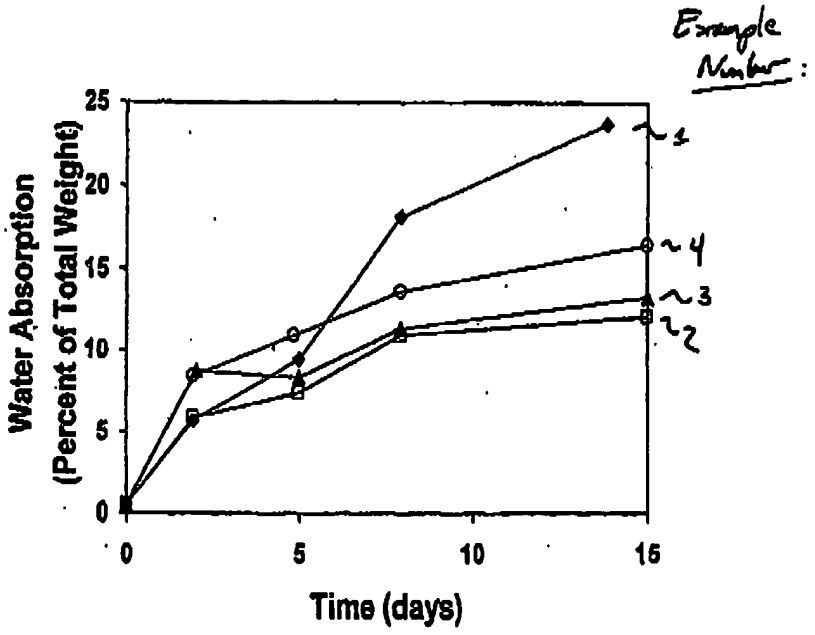

Figure 5 is a graph comparing protein release from the exemplary compositions. The rate of release of the protein is dependent on the relative amounts of crystallizable and amorphous polymer in these compositions. Figure 10 is a graph comparing the water absorbed by the exemplary compositions. The behavior of these compositions in an aqueous environment is also dependent on the relative amounts of crystallizable and amorphous polymer in the formulation.

The rejection of the claims over Mathiowitz et al., Shukla, and Brodbeck et al., alone or in combination, is respectfully traversed. Claims 1 and 34 include a biodegradable crystallizable polymer, a biodegradable amorphous polymer, a biocompatible solvent and a bioactive agent.

The examiner states that the term "crystallizable" is an intended use phrase. Applicants respectfully disagree with the examiner: the term "crystallizable" is a physical property of the polymer, as defined in the specification.

The present specification shows that the term "crystallizable" refers to "a polymer which has the ability to crystallize into ordered morphologies." (See Spec. page 4, lines 4-5). Crystallizable polymers, when crystallized, are semi-crystalline; and all semi-crystalline polymers are crystallizable. Thus, the term "crystallizable" is a physical property. This is not an intended use phrase and must be considered by the examiner.

Furthermore, polyester, polystyrene and polylactic acid are names of polymer classes. Many of these classes contain both amorphous and crystallizable polymers. Therefore, simply using a class name is not sufficient to determine whether a polymer is crystallizable. Thus, the term "crystallizable" does provide a specific parameter to distinguish the polymers.

When a claim is being considered, it must be considered "as a whole" in chemical cases. MPEP §2141.02, 2-5. This means that all relevant property differences must be considered in the light of the facts of each case. In the leading case of *In re Papesch*, the Court held that "patentability is not to be determined on the basis of structure alone and that from the standpoint of patent law, a compound and all of its properties are inseparabl ." MPEP § 2141.02 quoting *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963). In determining obviousness, the court has

frequently stated that properties of chemical compounds must be considered. *In re Huellmantel*, 324 F.2d 998, 1001, 139 USPQ 496 (CCPA 1963); *In re Lambooy*, 49 CCPA 985, 300 F.2d 950; *In re Petering and Fall*, 49 CCPA 993, 301 F.2d 676. Thus, the examiner cannot simply ignore the term "crystallizable".

Mathiowitz et al. describes multiwall polymeric microspheres. In the Examples only methylene chloride is used as the solvent. No other solvents are described. There is no suggestion that the solvent be biocompatabile; the solvent is always removed prior to use. Brodbeck et al. describes an implantable gel for drug delivery. The Examples describe biodegradable compositions containing biocompatable solvents. There is no description that the polymers in the list are either crystallizable or amorphous.

The claimed invention specifies the inclusion of a biocompatable solvent. The only solvent described by Mathiowitz et al. is methylene chloride, which is not biocompatable. There is no suggestion to use a biocomptable solvent, since there is no need as it is removed before use. Since Mathiowitz et al. always remove all the solvent prior to use, there would be no reason to use the biocompatable solvents of Brodbeck et al. Accordingly, the claimed invention is neither anticipated by, nor obvious over, these applied references.

Shukla describes a biodegradable vehicle and filler. The only description of crystallinity is in column 9, lines 28-36, and Example 29. These identical description list an infinite variety of composition, including blends of polymers and copolymers of varying molecular weights, copolymers of varying copolymer ratios and blends of polymers with varying hydrophobicity, lipophilicity or crystallinity. There is no specific description of a mixture of crystallizable and non-crystallizable polymers.

A generic formula does not anticipate a species when the generic formula encompasses a vast number and perhaps even an infinite number of compounds. MPEP § 2131.02, citing *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962). Shukla describes using blends of polymers and copolymer or blends of different types of polymers with varying hydrophobicity or lipophiliicty or crystallinity and it lists some examples of the ratios (col. 9, lines 32-36). However, the description in Shukla is not specific, even in Example 29, and never specifically states or suggests a mixture of

crystallizable and non-crystallizable polymers. Since Brodbeck et al. also fails to describe or suggest a combination of crystallizable and non-crystallizable polymers, the claimed invention is neither anticipated by, nor obvious over, the applied references.

Further evidence of unobviousness is provided by comparison of Examples 1-5 from the present application. These examples, and the associated Figures 5 and 10 reproduced above, illustrate the unexpected and surprising results obtained by the use of a biodegradable crystallizable polymer. Both the release of the bioactive agent and the water absorption characteristics can be varied by controlling the relative amounts of crystallizable polymer and amorphous polymer in the compositions. For example, the presence of a crystallizable polymer may provide for a rapid release of the bioactive agent. The type and relative amount of crystallizable polymer may affect both the timing and the amplitude of the rapid release. There is nothing in the applied references to suggest these results. These unexpected and surprising results demonstrate the unobviousness of the claimed invention.

Applicants submit that the claimed invention is neither anticipated by, nor obvious over, the applied references. Withdrawal of these rejections is respectfully requested.

Applicants submit that the application is in condition for allowance. Early notice of such action is respectfully requested.

Respectfully submitted,

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